

1           1.    A method for determining whether a test  
2 compound modulates the drug resistance of a cell, the method  
3 comprising:

4           a) determining the level of Chk1 expression in a  
5 cell in the presence of a test compound;

6           b) determining the level of Chk1 expression in the  
7 cell in the absence of the test compound; and

8           c) identifying the compound as a modulator of drug  
9 resistance of the cell if the level of expression of Chk1 in  
10 the cell in the presence of the test compound differs from  
11 the level of expression of Chk1 in the cell in the absence  
12 of the test compound.

1           2.    The method of claim 1 wherein the Chk1 is  
2 encoded by an endogenous gene.

1           3.    A method for determining whether a test  
2 compound modulates the drug resistance of a cell, the method  
3 comprising:

4           a) incubating Chk1 protein in the presence of a test  
5 compound;

6           b) determining whether the test compound binds to  
7 the Chk1 protein;

8           c) selecting a test compound which binds to the Chk1  
9 protein;

10          d) administering the test compound selected in step  
11 c) to a non-human mammal having drug resistant cells;

12          e) determining whether the test compound alters the  
13 drug resistance of the cells in the non-human mammal; and

14          f) identifying the test compound as a modulator of  
15 drug resistance of the cell if the compound alters the drug  
16 resistance of the cells in step e).

1           4.    A method for determining whether a test cell  
2 has a drug-resistant phenotype, the method comprising:  
3           a) measuring the expression of Chk1 in the test  
4 cell;  
5           b) comparing the expression of Chk1 measured in step  
6 a) to the expression of Chk1 in a control cell not having a  
7 drug-resistant phenotype; and  
8           c) determining that the test cell has a drug  
9 resistant phenotype if the expression of Chk1 in the test  
10 cell is greater than the expression of Chk1 in the control  
11 cell.

1           5.    A method of determining whether a test cell has  
2 a drug-resistant phenotype, the method comprising:  
3           a) measuring the activity of Chk1 in the test cell;  
4           b) comparing the activity of Chk1 measured in step  
5 a) to the activity of Chk1 in a control cell not having a  
6 drug-resistant phenotype; and  
7           c) determining that the test cell has a drug  
8 resistant phenotype if the activity of Chk1 in the test cell  
9 is greater than the activity of Chk1 in the control cell.

1           6.    A method for determining whether a subject has  
2 or is at risk of developing a drug resistant tumor, the  
3 method comprising:  
4           a) measuring the expression of Chk1 mRNA in a  
5 biological sample obtained from the subject;  
6           b) comparing the expression of Chk1 mRNA measured in  
7 step a) to the expression of Chk1 mRNA in a biological  
8 sample obtained from a control subject not having a drug  
9 resistant tumor; and  
10           c) determining that the patient has or is at risk of  
11 developing a drug resistant tumor if the expression of Chk1

12 mRNA in the biological sample obtained from the patient is  
13 higher than the expression of Chk1 mRNA in the biological  
14 sample obtained from the control subject.

1 7. The method of claim 6, wherein step a)  
2 comprises the use of a nucleic acid molecule that hybridizes  
3 to Chk1 mRNA.

1 8. A method for determining whether a subject has  
2 or is at risk of developing a drug resistant tumor, the  
3 method comprising:

4 a) measuring the activity of Chk1 in a biological  
5 sample obtained from the subject;

6 b) comparing the activity of Chk1 measured in step  
7 a) to the expression of Chk1 mRNA in a biological sample  
8 obtained from a control subject not having a drug resistant  
9 tumor; and

10 c) determining that the patient has or is at risk of  
11 developing a drug resistant tumor if the activity of Chk1 in  
12 the biological sample obtained from the patient is higher  
13 than the activity of Chk1 in the biological sample obtained  
14 from the control subject.

1 9. The method of claim 8, wherein step a)  
2 comprises the use of an agent that binds to Chk1 protein.

1 10. A method for monitoring the effect of an anti-  
2 tumor treatment on a patient, the method comprising:

3 a) measuring the expression of Chk1 in a tumor  
4 sample obtained from the patient;

5 b) comparing the expression of Chk1 measured in step  
6 a) to the expression of Chk1 in a control sample of cells;  
7 and

8           c) determining that the anti-tumor treatment should  
9 be discontinued or modified if the expression of Chk1 in the  
10 tumor sample is higher than the expression of Chk1 in the  
11 control sample of cells.

1           11. The method of claim 10, wherein step a)  
2 comprises the use of a nucleic acid molecule that hybridizes  
3 to Chk1 mRNA.

1           12. A method for monitoring the effect of an anti-  
2 tumor treatment on a patient, the method comprising:  
3           a) measuring the activity of Chk1 in a tumor sample  
4 obtained from the patient;  
5           b) comparing the activity of Chk1 measured in step  
6 a) to the activity of Chk1 in a control sample of cells; and  
7           c) determining that the anti-tumor treatment should  
8 be discontinued or modified if the activity of Chk1 in the  
9 tumor sample is higher than the activity of Chk1 in the  
10 control sample of cells.

1           13. The method of claim 12, wherein step a)  
2 comprises the use of an agent that binds to Chk1 protein.

1           14. A method for modulating the drug resistance of  
2 a cell, the method comprising modulating Chk1 expression  
3 within the cell.

1           15. A method reducing the drug resistance of cell,  
2 the method comprising contacting the cell with a molecule  
3 which reduces the expression of Chk1 within the cell.

1           16. A method of increasing the effectiveness of a  
2 chemotherapeutic compound in a patient suffering from a

3 disorder associated with the presence of drug-resistant  
4 neoplastic cells, the method comprising:  
5 a) administering a chemotherapeutic compound to the  
6 patient; and  
7 b) administering a compound with reduces Chk1  
8 expression to the patient.

1 17. A method of treating a mammal suspected of  
2 having a disorder associated with the presence of drug-  
3 resistant cells, the method comprising administering to the  
4 mammal a compound that reduces the expression of Chk1 in the  
5 drug-resistant cells, the reduction be sufficient to reduce  
6 the drug resistance of the drug resistant cells.

1 18. A method for increasing the drug resistance of  
2 cell that has an undesirably low level of Chk1 expression,  
3 the method comprising exposing the cell to a compound that  
4 increases the expression of Chk1.

1 19. A method for treating a drug resistant tumor in  
2 a patient, the method comprising administering to said  
3 subject an amount of a Chk1 antagonist effective to reduce  
4 drug resistance of said tumor in the patient.

1 20. The use of an inhibitor of Chk1 expression, or  
2 pharmaceutically acceptable salt thereof, or a  
3 pharmaceutical composition containing either entity, for the  
4 manufacture of a medicament for the treatment of a drug  
5 resistant tumor in a patient.